

## General

## Guideline Title

Evidence-based guideline: treatment of tardive syndromes: report of the Guideline Development Subcommittee of the American Academy of Neurology.

## Bibliographic Source(s)

Bhidayasiri R, Fahn S, Weiner WJ, Gronseth GS, Sullivan KL, Zesiewicz TA. Evidence-based guideline: treatment of tardive syndromes: report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology. 2013 Jul 30;81(5):463-9. [40 references] PubMed

#### **Guideline Status**

This is the current release of the guideline.

# Regulatory Alert

## FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

•	August 31, 2016 – Opioid pain and cough medicines combined with benzodiazepines : A U.S. Food and Drug
	Administration (FDA) review has found that the growing combined used of opioid medicines with benzodiazepines or other drugs that
	depress the central nervous system (CNS) has resulted in serious side effects, including slowed or difficult breathing and deaths. FDA is
	adding Boxed Warnings to the drug labeling of prescription opioid pain and prescription opioid cough medicines and benzodiazepines.
•	May 10, 2016 – Olanzapine : The U.S. Food and Drug Administration (FDA) is warning that the antipsychotic
	medicine olanzapine can cause a rare but serious skin reaction that can progress to affect other parts of the body. FDA is adding a new
	warning to the drug labels for all olanzapine-containing products that describes this severe condition known as Drug Reaction with
	Eosinophilia and Systemic Symptoms (DRESS).
•	May 3, 2016 – Aripiprazole (Abilify, Abilify Maintena, Aristada) : The U.S. Food and Drug Administration (FDA
	is warning that compulsive or uncontrollable urges to gamble, binge eat, shop, and have sex have been reported with the use of the
	antipsychotic drug aripiprazole (Abilify, Abilify Maintena, Aristada, and generics). These uncontrollable urges were reported to have
stopped when the medicine was discontinued or the dose was reduced. These impulse-control problems are rare, but the	
	harm to the patient and others if not recognized.

# Recommendations

### Major Recommendations

Definitions of the levels of the recommendations (A, B, C, U) and classification of the evidence (Class I-IV) are provided at the end of the "Major Recommendations" field.

Is Withdrawal of Dopamine Receptor Blocking Agents (DRBAs) an Effective Tardive Syndrome (TDS) Treatment?

Conclusion and Recommendation

Data are insufficient to support or refute TDS treatment by DRBA withdrawal (Level U).

Clinical Context

The American Psychiatric Association Task Force recommends antipsychotic withdrawal only in patients who can tolerate it. Despite limited evidence, clinical impression indicates that short-term withdrawal may worsen dyskinesias, whereas adding antipsychotics with stronger extrapyramidal symptoms can reduce TDS. Psychotic relapse predictors include younger age, higher baseline antipsychotic dosage, and shorter hospitalization.

Does Switching from Typical to Atypical DRBAs Reduce TDS Symptoms?

Conclusion and Recommendation

Data are insufficient to support or refute TDS treatment by changing to atypical antipsychotics (Level U, Class IV studies).

What Is the Efficacy of Pharmacologic Agents in Treating TDS?

Acetazolamide and Amantadine

Conclusions

Acetazolamide and thiamine reduced TDS in one Class III study. Amantadine reduced TDS when used conjointly with a neuroleptic during the first 7 weeks (1 Class II study, 2 Class III studies).

Recommendations

Data are insufficient to support or refute TDS treatment with acetazolamide and thiamine (Level U). Amantadine with neuroleptics may be considered to treat TDS for short-term use (Level C).

Clinical Context

Only flupentixol decanoate, chlorpromazine, haloperidol, trifluoperazine, and thioridazine were tested with amantadine in these studies. The efficacy of amantadine plus other neuroleptics in TDS treatment is unknown. Because safety data are unavailable concerning long-term use of only typical neuroleptics as TDS suppressive agents and because of these agents' propensity to cause TDS, the evidence suggests only potential efficacy short-term.

First-Generation Antipsychotics

Conclusions

Haloperidol possibly reduces TDS movements for up to 2 weeks (2 Class II studies, 1 Class III study) but is associated with increased akinetic-rigid syndrome (1 Class II study). Data are insufficient to support or refute the use of thiopropazate in reducing oral dyskinesia (1 Class III study).

Recommendations

Data are insufficient to support or refute the use of thiopropazate, molindone, sulpiride, fluperlapine, and flupenthixol in treating TDS (Level U).

Clinical Context

Although haloperidol and thiopropazate possibly reduce TDS, they are not recommended because of the competing risk of akinetic-rigid syndrome. Safety data are unavailable concerning long-term use of typical antipsychotics as TDS suppressive agents, and these drugs themselves can cause TDS; these significant risks outweigh the benefits of any short-term use of typical antipsychotics.

Second-Generation Antipsychotics: Clozapine, Risperidone, Olanzapine, and Other Agents

Conclusions

Data are conflicting regarding the use of clozapine (conflicting Class III studies). Risperidone (2 Class III studies, 1 Class III study) is probably effective in reducing tardive dyskinesia (TDD). Olanzapine is possibly effective in reducing TDD (2 Class III studies). The safety of risperidone and olanzapine as a TDS suppressant for use beyond 48 weeks has not been addressed.

There is no evidence to determine the efficacy of quetiapine, ziprasidone, aripiprazole, and sertindole in TDS treatment.

Recommendations

Because neuroleptic agents may themselves cause TDS and may mask its symptoms rather than treat it, these drugs cannot be recommended for TDS treatment (Level U). Caution is advised when using risperidone or olanzapine to reduce TDS.

Electroconvulsive Therapy

Conclusion and Recommendation

Data are insufficient to determine the efficacy of electroconvulsive therapy for TDD treatment (Level U).

Dopamine-Depleting Agents: Tetrabenazine, Reserpine, and α-Methyldopa

Conclusions

Tetrabenazine (TBZ) possibly reduces TDS symptoms (2 consistent Class III studies). One study (Class III) found reserpine and  $\alpha$ -methyldopa effective in treating TDS.

Recommendations

TBZ may be considered in treating TDS (Level C). Data are insufficient to determine the efficacy of reserpine or  $\alpha$ -methyldopa in treating TDS (Level U).

Clinical Context

TBZ reduces TDS symptoms; there is no evidence that long-term TBZ administration induces TDS, but it can cause parkinsonism.

Dopamine Agonists

Conclusion and Recommendation

Data are insufficient to support or refute the use of bromocriptine for TDS treatment (Level U).

Cholinergic Drugs

Conclusion

Galantamine is possibly ineffective in treating TDS (1 Class II study).

Recommendations

Galantamine might not be considered in treating TDS (Level C). Data are insufficient to determine the effectiveness of other cholinergic drugs in treating TDS (Level U).

Anticholinergic Drugs

Conclusion and Recommendation

Data are insufficient to determine the effectiveness of anticholinergic drugs in treating TDS (Level U).

Biperiden (Akineton) Discontinuation

Conclusion and Recommendation

Data are insufficient to determine the effectiveness of biperiden discontinuation in treating TDS (Level U, 1 Class III study).

Antioxidants

Conclusions and Recommendations

EGb-761 is probably useful in TDS treatment (1 Class I study), but data are limited to inpatients with schizophrenia (Level B).

Based on 4 Class II and numerous Class III studies, data are conflicting regarding vitamin E efficacy in treating TDS. Data are insufficient to determine the efficacy of vitamin E (Level U).

Based on 1 Class II study, eicosapentaenoic acid (EPA) is possibly ineffective in treating TDS and might not be considered (Level C).

Melatonin is possibly ineffective in treating TDS at a 2-mg/d dose (1 Class II study) but is possibly effective in treating TDS at a 10-mg/d dose (1 Class II study). Evidence regarding TDS treatment with melatonin is conflicting (Level U).

Data are insufficient to support or refute the use of other antioxidants, including vitamin B<sub>6</sub>, selegiline, and yi-gan san, in treating TDS (Level U).

γ-Aminobutyric Acid (GABA) Agonists

Conclusions and Recommendations

Based on 1 Class I study, clonazepam is probably effective in decreasing TDD symptoms short-term (approximately 3 months) and should be considered for short-term TDD treatment (Level B). Data are insufficient to support or refute baclofen use in treating TDD (Level U).

Levetiracetam

Conclusion and Recommendation

Data are insufficient to recommend levetiracetam as TDS treatment (Level U, 1 Class III study).

Calcium Channel Blockers

Conclusions and Recommendations

Data are insufficient to support or refute nifedipine use in treating TDD (Level U). Diltiazem probably does not reduce TDD and should not be considered as treatment (Level B, 1 Class I study).

Buspirone

Conclusion and Recommendation

Data are insufficient to support or refute buspirone use in treating TDD (Level U, 1 Class III study).

Do Patients with TDS Benefit From Chemodenervation with Botulinum Toxin (BoNT)?

Conclusion and Recommendation

Data are insufficient to support or refute BoNT use to treat TDS symptoms (Level U).

Do Patients with TDS Benefit From Surgical Therapy?

Conclusion and Recommendation

Data are insufficient to support or refute pallidal deep brain stimulation (DBS) use in treating TDS (Level U, Class IV studies).

**Definitions**:

Classification of Evidence for Therapeutic Articles

Class I: A randomized, controlled clinical trial of the intervention of interest with masked or objective outcome assessment, in a representative population. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences.

The following are also required:

- a. Concealed allocation
- b. Primary outcome(s) clearly defined

- c. Exclusion/inclusion criteria clearly defined
- d. Adequate accounting for dropouts (with at least 80% of enrolled subjects completing the study) and crossovers with numbers sufficiently low to have minimal potential for bias.
- e. For noninferiority or equivalence trials claiming to prove efficacy for one or both drugs, the following are also required\*
  - The authors explicitly state the clinically meaningful difference to be excluded by defining the threshold for equivalence or noninferiority.
  - 2. The standard treatment used in the study is substantially similar to that used in previous studies establishing efficacy of the standard treatment (e.g., for a drug, the mode of administration, dose and dosage adjustments are similar to those previously shown to be effective).
  - 3. The inclusion and exclusion criteria for patient selection and the outcomes of patients on the standard treatment are comparable to those of previous studies establishing efficacy of the standard treatment.
  - 4. The interpretation of the results of the study is based upon a per protocol analysis that takes into account dropouts or crossovers.

Class II: A randomized, controlled clinical trial of the intervention of interest in a representative population with masked or objective outcome assessment that lacks one criterion from a—e above or a prospective matched cohort study with masked or objective outcome assessment in a representative population that meets b—e above. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences.

Class III: All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome is independently assessed, or independently derived by objective outcome measurement.\*\*

Class IV: Studies not meeting Class I, II or III criteria including consensus or expert opinion.

\*Note that numbers 1-3 in Class Ie are required for Class II in equivalence trials. If any one of the three is missing, the class is automatically downgraded to Class III.

\*\*Objective outcome measurement: an outcome measure that is unlikely to be affected by an observer's (patient, treating physician, investigator) expectation or bias (e.g., blood tests, administrative outcome data).

#### Classification of Recommendations

A = Established as effective, ineffective or harmful (or established as useful/predictive or not useful/predictive) for the given condition in the specified population. (Level A rating requires at least two consistent Class I studies.)\*

B = Probably effective, ineffective or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified population. (Level B rating requires at least one Class I study or two consistent Class II studies.)

C = Possibly effective, ineffective or harmful (or possibly useful/predictive or not useful/predictive) for the given condition in the specified population. (Level C rating requires at least one Class II study or two consistent Class III studies.)

U = Data inadequate or conflicting; given current knowledge, treatment (test, predictor) is unproven.

\*In exceptional cases, one convincing Class I study may suffice for an "A" recommendation if 1) all criteria are met, 2) the magnitude of effect is large (relative rate improved outcome >5 and the lower limit of the confidence interval is >2).

## Clinical Algorithm(s)

None provided

# Scope

## Disease/Condition(s)

Tardive syndromes (TDS), including tardive dyskinesias (TDD)

# Guideline Category

Management

# Clinical Specialty

Neurology

#### Intended Users

Advanced Practice Nurses

Physician Assistants

Physicians

### Guideline Objective(s)

To make evidence-based recommendations regarding management of tardive syndromes (TDS), including tardive dyskinesias (TDD), by addressing five questions:

- 1. Is withdrawal of dopamine receptor blocking agents (DRBAs) an effective TDS treatment?
- 2. Does switching from typical to atypical DRBAs reduce TDS symptoms?
- 3. What is the efficacy of pharmacologic agents in treating TDS?
- 4. Do patients with TDS benefit from chemodenervation with botulinum toxin (BoNT)?
- 5. Do patients with TDS benefit from surgical therapy?

### **Target Population**

Adult patients presenting with tardive syndromes (TDS), including tardive dyskinesias (TDD)

### Interventions and Practices Considered

- 1. Withdrawal of dopamine receptor blocking agents (DRBAs)
- 2. Switching from typical to atypical DRBAs
- 3. Pharmacological agents
  - Acetazolamide
  - Amantadine
  - First-generation antipsychotics (haloperidol, thiopropazate, molindone, sulpiride, fluperlapine and flupenthixol)
  - Second-generation antipsychotics (clozapine, risperidone, olanzapine, and other neuroleptic agents)
  - Electroconvulsive therapy
  - Dopamine-depleting agents (tetrabenazine [TBZ], reserpine, and α-methyldopa)
  - Dopamine agonists
  - Cholinergic drugs
  - Anticholinergic drugs
  - Biperiden (Akineton) discontinuation
  - Antioxidants
  - γ-Aminobutyric acid (GABA) agonists
  - Levetiracetam
  - Calcium channel blockers
  - Buspirone
- 4. Chemodenervation with botulinum toxin (BoNT)
- 5. Surgical therapy (pallidal deep brain stimulation [DBS])

## Major Outcomes Considered

Improvement on objective clinical rating scales of tardive syndromes (TDS) severity (e.g., Abnormal Involuntary Movement Scale [AIMS])

# Methodology

#### Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

### Description of Methods Used to Collect/Select the Evidence

PsycINFO, Ovid MEDLINE, EMBASE, Web of Science, and Cochrane were searched (1966–2011) (see appendices e-3–e-7 of the data supplement [see the "Availability of Companion Documents field"]). The search was supplemented using the bibliography of retrieved articles and panelists' knowledge and following the American Academy of Neurology's (AAN's) process manual. The authors included studies of the following tardive syndrome (TDS) treatments: neuroleptic withdrawal, anticholinergics, benzodiazepines, β-blockers, calcium channel blockers, cholinergics, GABAergic compounds, neuroleptic medications (including dose reduction and cessation), non-neuroleptic compounds that affect the dopamine and noradrenaline systems, vitamin B6, and vitamin E. The preferred outcome measures are objective clinical rating scales of TDS severity (e.g., Abnormal Involuntary Movement Scale [AIMS]). Two panelists reviewed abstracts and titles for relevance.

#### Number of Source Documents

Not stated

## Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

## Rating Scheme for the Strength of the Evidence

Classification of Evidence for Therapeutic Articles

Class I: A randomized, controlled clinical trial of the intervention of interest with masked or objective outcome assessment, in a representative population. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences.

The following are also required:

- a. Concealed allocation
- b. Primary outcome(s) clearly defined
- c. Exclusion/inclusion criteria clearly defined
- d. Adequate accounting for dropouts (with at least 80% of enrolled subjects completing the study) and crossovers with numbers sufficiently low to have minimal potential for bias.
- e. For noninferiority or equivalence trials claiming to prove efficacy for one or both drugs, the following are also required\*
  - 1. The authors explicitly state the clinically meaningful difference to be excluded by defining the threshold for equivalence or noninferiority.

- 2. The standard treatment used in the study is substantially similar to that used in previous studies establishing efficacy of the standard treatment (e.g., for a drug, the mode of administration, dose and dosage adjustments are similar to those previously shown to be effective).
- 3. The inclusion and exclusion criteria for patient selection and the outcomes of patients on the standard treatment are comparable to those of previous studies establishing efficacy of the standard treatment.
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Class II: A randomized, controlled clinical trial of the intervention of interest in a representative population with masked or objective outcome assessment that lacks one criterion from a—e above or a prospective matched cohort study with masked or objective outcome assessment in a representative population that meets b—e above. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences.

Class III: All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome is independently assessed, or independently derived by objective outcome measurement.\*\*

Class IV: Studies not meeting Class I, II or III criteria including consensus or expert opinion.

\*Note that numbers 1-3 in Class Ie are required for Class II in equivalence trials. If any one of the three is missing, the class is automatically downgraded to Class III.

\*\*Objective outcome measurement: an outcome measure that is unlikely to be affected by an observer's (patient, treating physician, investigator) expectation or bias (e.g., blood tests, administrative outcome data).

## Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

## Description of the Methods Used to Analyze the Evidence

Two panelists reviewed abstracts and titles for relevance and rated selected studies using the American Academy of Neurology (AAN) therapeutic classification scheme (see the "Rating Scheme for the Strength of the Evidence" field).

See Table e-1 in the data supplement for a summary of the evidence (see the "Availability of Companion Documents" field).

### Methods Used to Formulate the Recommendations

Expert Consensus

## Description of Methods Used to Formulate the Recommendations

Recommendations were linked to the evidence (see the "Rating Scheme for the Strength of the Recommendations" field). Disagreements regarding classification were resolved by consensus.

## Rating Scheme for the Strength of the Recommendations

Classification of Recommendations

A = Established as effective, ineffective or harmful (or established as useful/predictive or not useful/predictive) for the given condition in the specified population. (Level A rating requires at least two consistent Class I studies.)\*

B = Probably effective, ineffective or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified population. (Level B rating requires at least one Class I study or two consistent Class II studies.)

C = Possibly effective, ineffective or harmful (or possibly useful/predictive or not useful/predictive) for the given condition in the specified population. (Level C rating requires at least one Class II study or two consistent Class III studies.)

U = Data inadequate or conflicting; given current knowledge, treatment (test, predictor) is unproven.

\*In exceptional cases, one convincing Class I study may suffice for an "A" recommendation if 1) all criteria are met, 2) the magnitude of effect is large (relative rate improved outcome >5 and the lower limit of the confidence interval is >2).

### Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

### Method of Guideline Validation

External Peer Review

Internal Peer Review

### Description of Method of Guideline Validation

Drafts of the guideline have been reviewed by at least 3 American Academy of Neurology (AAN) committees, a network of neurologists, Neurology® peer reviewers, and representatives from related fields.

The original guideline document was approved by the Guideline Development Subcommittee on January 21, 2012; by the Practice Committee on October 1, 2012; and by the AAN Board of Directors on April 25, 2013.

# **Evidence Supporting the Recommendations**

## Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

# Benefits/Harms of Implementing the Guideline Recommendations

### **Potential Benefits**

Appropriate medical and surgical management of patients with tardive syndromes (TDS)

### **Potential Harms**

Some of the drugs described in the guideline may have serious side effects or other risks associated with them. Refer to the "Major Recommendations" field and the original guideline document for specific recommendations and clinical context.

# **Qualifying Statements**

## **Qualifying Statements**

This statement is provided as an educational service of the American Academy of Neurology (AAN). It is based on an assessment of current scientific and clinical information. It is not intended to include all possible proper methods of care for a particular neurologic problem or all legitimate criteria for choosing to use a specific procedure. Neither is it intended to exclude any reasonable alternative methodologies. The AAN recognizes that specific patient care decisions are the prerogative of the patient and the physician caring for the patient, based on all of the

circumstances involved. The clinical context section is made available in order to place the evidence-based guideline(s) into perspective with current practice habits and challenges. Formal practice recommendations are not intended to replace clinical judgment.

# Implementation of the Guideline

### Description of Implementation Strategy

An implementation strategy was not provided.

## **Implementation Tools**

Patient Resources

Quick Reference Guides/Physician Guides

Resources

Slide Presentation

Staff Training/Competency Material

For information about availability, see the Availability of Companion Documents and Patient Resources fields below.

# Institute of Medicine (IOM) National Healthcare Quality Report Categories

#### IOM Care Need

Getting Better

Living with Illness

### **IOM Domain**

Effectiveness

# Identifying Information and Availability

## Bibliographic Source(s)

Bhidayasiri R, Fahn S, Weiner WJ, Gronseth GS, Sullivan KL, Zesiewicz TA. Evidence-based guideline: treatment of tardive syndromes: report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology. 2013 Jul 30;81(5):463-9. [40 references] PubMed

## Adaptation

Not applicable: the guideline was not adapted from another source.

#### Date Released

2013 Jul 30

### Guideline Developer(s)

American Academy of Neurology - Medical Specialty Society

### Source(s) of Funding

American Academy of Neurology (AAN)

### Guideline Committee

Guideline Development Subcommittee of the American Academy of Neurology

## Composition of Group That Authored the Guideline

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### Financial Disclosures/Conflicts of Interest

#### Conflict of Interest

The American Academy of Neurology (AAN) is committed to producing independent, critical, and truthful clinical practice guidelines (CPGs). Significant efforts are made to minimize the potential for conflicts of interest to influence the recommendations of this CPG. To the extent possible, the AAN keeps separate those who have a financial stake in the success or failure of the products appraised in the CPGs and the developers of the guidelines. Conflict of interest forms were obtained from all authors and reviewed by an oversight committee prior to project initiation. AAN limits the participation of authors with substantial conflicts of interest. The AAN forbids commercial participation in, or funding of, guideline projects. Drafts of the guideline have been reviewed by at least 3 AAN committees, a network of neurologists, *Neurology*® peer reviewers, and representatives from related fields. The AAN Guideline Author Conflict of Interest Policy can be viewed at www.aan.com

#### Disclosures

- R. Bhidayasiri is supported by the Rachadaphiseksomphot Endowment Fund part of the "Strengthen CUs Researchers Project" and research unit grant number GRU 52-026-30-005 of Chulalongkorn University, Bangkok, Thailand.
- S. Fahn reports no disclosures.
- W. Weiner is deceased; disclosures are not included for this author.
- G. Gronseth and K. Sullivan report no disclosures.
- T. Zesiewicz has received research funding from Boehringer-Ingelheim, Novartis, GlaxoSmithKline, Teva Neuroscience, General Electric, UCB

Pharma, and the Friedreich's Ataxia Res	Catch Amarice.
Go to Neurology.org	for full disclosures.
Guideline Status	
This is the current release of the guideline	3.
Guideline Availability	
Electronic copies: A list of American Act this guideline, is available at the AAN W	ademy of Neurology (AAN) guidelines, along with a link to a Portable Document Format (PDF) file for reb site
Print copies: Available from the AAN M 55415.	Iember Services Center, (800) 879-1960, or from AAN, 201 Chicago Avenue South, Minneapolis, MN
Availability of Companio	n Documents
The following are available:	
American Academy of Neurology  Evidence-based guideline: treatme Electronic copies: Available from  Evidence-based guideline: treatme American Academy of Neurology  Evidence-based guideline: treatme Electronic copies: Available from  Evidence-based guideline: treatme copies: Available from the AAN V	ent of tardive syndromes. AAN summary of evidence-based guideline for clinicians. St. Paul (MN): v. 2013; 3 p. Electronic copies: Available from the AAN Web site ent of tardive syndromes. Case study. St. Paul (MN): American Academy of Neurology. 2013; 7 p. the AAN Web site ent of tardive syndromes. Podcast. St. Paul (MN): American Academy of Neurology; 2013. Electronic
Patient Resources	
The following is available:	
Academy of Neurology. 2013. 3	ndromes. Summary of evidence-based guideline for patients and their families. St. Paul (MN): American p. Electronic copies: Available from the American Academy of Neurology (AAN) Web site o provide health professionals with information to share with their patients to help them better understand their health and their

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

### **NGC Status**

This summary was completed by ECRI Institute on November 18, 2013. This summary was updated by ECRI Institute on May 24, 2016 following the U.S. Food and Drug Administration advisory on Olanzapine. This summary was updated by ECRI Institute on May 31, 2016 following the U.S. Food and Drug Administration advisory on Aripiprazole (Abilify, Abilify Maintena, Aristada). This summary was updated by ECRI Institute on October 21, 2016 following the U.S. Food and Drug Administration advisory on opioid pain and cough medicines combined

with benzodiazepines.

## Copyright Statement

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# Disclaimer

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